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☐	L1	microarray same principal component analysis	11

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NEWS 19	DEC 22	ABI-INFORM now available on STN
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NEWS 21	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS 22	FEB 05	German (DE) application and patent publication number format changes
NEWS 23	MAR 03	MEDLINE and LMEDLINE reloaded
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FILE 'HOME' ENTERED AT 14:59:29 ON 18 MAR 2004

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FILE 'MEDLINE' ENTERED AT 15:12:54 ON 18 MAR 2004

FILE 'BIOSIS' ENTERED AT 15:12:54 ON 18 MAR 2004

=> s principal component analysis and microarray
L1 133 PRINCIPAL COMPONENT ANALYSIS AND MICROARRAY

=> s l1 and toxic?
L2 14 L1 AND TOXIC?

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L3 ANSWER 1 OF 10 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:190642 BIOSIS
DN PREV200300190642
TI **Toxicogenomics** of bromobenzene hepatotoxicity: A combined transcriptomics and proteomics approach.
AU Heijne, Wilbert H. M. [Reprint Author]; Stierum, Rob H.; Slijper, Monique; van Bladeren, Peter J.; van Ommen, Ben
CS TNO Nutrition and Food Research, 3700 AJ, P.O. Box 360, Zeist, Netherlands heijne@voeding.tno.nl
SO Biochemical Pharmacology, (1 March 2003) Vol. 65, No. 5, pp. 857-875. print.
CODEN: BCPCA6. ISSN: 0006-2952.
DT Article
LA English
ED Entered STN: 16 Apr 2003
Last Updated on STN: 16 Apr 2003
AB **Toxicogenomics** is a novel approach integrating the expression analysis of thousands of genes (transcriptomics) or proteins (proteomics) with classical methods in **toxicology**. Effects at the molecular level are related to pathophysiological changes of the organisms, enabling

detailed comparison of mechanisms and early detection and prediction of **toxicity**. This report addresses the value of the combined use of transcriptomics and proteomics technologies in **toxicology**.
Acute hepatotoxicity was induced in rats by bromobenzene administration resulting in depleted glutathione levels and reduced average body weights, 24 hr after dosage. These physiological symptoms coincided with many changes of hepatic mRNA and protein content. Gene induction confirmed involvement of glutathione-S-transferase isozymes and epoxide hydrolase in bromobenzene metabolism and identified many genes possibly relevant in bromobenzene **toxicity**. Observed glutathione depletion coincided with induction of the key enzyme in glutathione biosynthesis, gamma-glutamylcysteine synthetase. Oxidative stress was apparent from strong upregulation of heme oxygenase, peroxiredoxin 1 and other genes. Bromobenzene-induced protein degradation was suggested from two-dimensional gel electrophoresis, upregulated mRNA levels for proteasome subunits and lysosomal cathepsin L, whereas also genes were upregulated with a role in protein synthesis. Both protein and gene expression profiles from treated rats were clearly distinct from controls as shown by **principal component analysis**,
and several proteins found to significantly change upon bromobenzene treatment were identified by mass spectrometry. A modest overlap in results from proteomics and transcriptomics was found. This work indicates that transcriptomics and proteomics technologies are complementary to each other and provide new possibilities in molecular **toxicology**.

=> d 2-10 bib ab

L3 ANSWER 2 OF 10 MEDLINE on STN DUPLICATE 1
AN 2003154112 MEDLINE
DN PubMed ID: 12670486
TI A method to improve selection of molecular targets by circumventing the ADME pharmacokinetic system utilizing PharmArray DNA **microarrays**
.
AU Dooley Thomas P; Curto Ernest V; Reddy Shanker P; Davis Richard L; Lambert Glenna; Wilborn Teresa W
CS IntegriDerm Inc., 2800 Milan Court, Birmingham, AL 35211-6908, USA.. dooley@intergriderm.com
NC R01-GM61399 (NIGMS)
SO Biochemical and biophysical research communications, (2003 Apr 11) 303 (3) 828-41.
Journal code: 0372516. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200305
ED Entered STN: 20030403
Last Updated on STN: 20030530
Entered Medline: 20030529
AB DNA **microarrays** may be used to identify potential molecular targets for drug discovery. Yet, DNA **microarray** experiments provide massive amounts of data. To limit the choice of potential molecular targets, it may be desirable to eliminate genes coincidentally up-regulated in tissues implicated in absorption, distribution, metabolism, and excretion (ADME) pharmacokinetics. DNA **microarray** experiments were performed to demonstrate a gene-exclusion approach using as an example RNA samples of neural origin, i.e., a human neuroblastoma cell line (SK-N-SH) and brain tissue, as the intended hypothetical site(s) of drug action. Biomarkers were identified using PharmArray DNA **microarrays**. The lists of neuroblastoma and neural biomarkers

were constrained by limiting selection to the subset of genes that were not highly expressed in three transformed cell lines from liver, colon, and kidney (HepG2, Caco-2, and 786-O, respectively) that are routinely used as representatives of the ADME system during in vitro pharmacology and **toxicology** experiments. **Principal component analysis** methods with likelihood ratio-related bioinformatic tools were utilized to identify robust potential biomarker genes for the three ADME-related cell lines, neuroblastoma, and normal brain. Biomarkers of each sample were identified and selected genes were validated by qRT-PCR. Hundreds of biomarkers of the three ADME-related cell types, representing hepatocytes, kidney epithelium, and gastrointestinal tract, may now be used as a valuable database to restrict selection of biomarkers as potential molecular targets from the intended samples (e.g., neuroblastoma in this work). In addition to biomarker discovery per se, this demonstration suggests that our model method may be viable to help restrict gene lists during selection of potential molecular targets for subsequent drug discovery.

L3 ANSWER 3 OF 10 MEDLINE on STN
AN 2003322200 MEDLINE
DN PubMed ID: 12851107
TI Transcription profiling distinguishes dose-dependent effects in the livers of rats treated with clofibrate.
AU Kramer Jeffrey A; Blomme Eric A G; Bunch Roderick T; Davila Julio C; Jackson Carmen J; Jones Patrick F; Kolaja Kyle L; Curtiss Sandra W
CS Pharmacia Corporation, Global Toxicology, 800 N. Lindbergh Blvd., St Louis, Missouri 63167, USA.. jeffrey.a.kramer@pharmacia.com
SO Toxicologic pathology, (2003 Jul-Aug) 31 (4) 417-31.
Journal code: 7905907. ISSN: 0192-6233.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200403
ED Entered STN: 20030710
Last Updated on STN: 20040311
Entered Medline: 20040310
AB Peroxisome proliferators such as the fibrates act via the peroxisome proliferator activated receptor (PPAR)-alpha as hypolipidemic agents. Many peroxisome proliferators are also nongenotoxic hepatic carcinogens and hepatotoxicants in rodents. We performed transcription profiling using cDNA **microarrays** on livers of rats treated for 5 days with 3 doses of the peroxisome proliferator clofibrate. All 3 doses had hepatic effects as assessed by liver to body weight ratio, alanine aminotransferase (ALT) increases and histopathology examination. Analysis of the transcription profiling data identified changes in the expression of many genes within several mechanistic pathways that support existing hypotheses regarding peroxisome proliferator mediated carcinogenicity. Additionally, the transcription profiling, histopathology, and clinical chemistry results suggested a biphasic response to clofibrate. These findings provide insight into the pathogenesis of **toxic** and carcinogenic effects of clofibrate in rodents and demonstrate the ability of cDNA **microarrays** to provide information regarding mechanisms of **toxicity** identified during the drug development process.

L3 ANSWER 4 OF 10 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:220580 BIOSIS
DN PREV200300220580
TI Comparative study of DNA **microarray** data analysis: **Principal Component Analysis** verses Fisher Linear Discriminant Analysis.
AU Stevenson, M. D. [Reprint Author]; Chan, V.; Gustafson, S.;

Kelley-Loughnane, N.; Harker, B. [Reprint Author]; Rudnicki, D. [Reprint Author]; Hussain, S.; Wang, C.; Frazier, J. [Reprint Author]

CS Operational Toxicology Branch, US Air Force, Wright-Patterson Air Force Base, OH, USA

SO Toxicological Sciences, (March 2003) Vol. 72, No. S-1, pp. 92. print.
Meeting Info.: 42nd Annual Meeting of the Society of Toxicology. Salt Lake City, Utah, USA. March 09-13, 2003. Society of Toxicology.
ISSN: 1096-6080 (ISSN print).

DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 7 May 2003
Last Updated on STN: 7 May 2003

L3 ANSWER 5 OF 10 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN 2003:546683 BIOSIS

DN PREV200300545506

TI Application of gene expression toward discovery of candidate biomarkers of nephrotoxicity: A collaboration within the International Life Sciences Institute consortium.

AU ILSI/HESI Genomics Nephrotoxicity Working Group

SO Toxicology Letters (Shannon), (September 2003) Vol. 144, No. Suppl. 1, pp. s55. print.
Meeting Info.: 41st Congress of the European Societies of Toxicology EUROTOX 2003 ' Science for Safety'. Florence, Italy. September 28-October 01, 2003.
CODEN: TOLED5. ISSN: 0378-4274.

DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 19 Nov 2003
Last Updated on STN: 19 Nov 2003

L3 ANSWER 6 OF 10 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN 2003:517149 BIOSIS

DN PREV200300519771

TI Host cellular responses to the cytotoxic enterotoxin of Aeromonas hydrophila: A **microarray** approach.

AU Galindo, C. L. [Reprint Author]; Sha, J. [Reprint Author]; Fadl, A. [Reprint Author]; Chopra, A. K. [Reprint Author]

CS Medical Branch, University of Texas, Galveston, TX, USA

SO Abstracts of the General Meeting of the American Society for Microbiology, (2003) Vol. 103, pp. B-017. http://www.asmusa.org/mtgsrc/generalmeeting.htm. cd-rom.
Meeting Info.: 103rd American Society for Microbiology General Meeting. Washington, DC, USA. May 18-22, 2003. American Society for Microbiology.
ISSN: 1060-2011 (ISSN print).

DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 5 Nov 2003
Last Updated on STN: 5 Nov 2003

AB The cytotoxic enterotoxin (Act) of A. hydrophila possesses several biological activities, including hemolysis, cytotoxicity, enterotoxicity, and lethality. The ability of Act to evoke an inflammatory response has been demonstrated, but the signal transduction pathways involved remain to be elucidated. In this study, we have utilized DNA array technology to gain a more global view of the cellular transcriptional responses to Act and to identify potentially important genes up-regulated by this toxin. A macrophage cell line (RAW 264.7) was treated with 6 ng/ml of Act, and the RNA was isolated at 0, 2, and 12 hr and applied to Affymetrix MGU74 arrays. Using a multi-analysis approach (MAS 5.0, SAM, GeneSpring, and

ANOVA), we identified fifty genes that were significantly and consistently up-regulated by the treatment. Many of these genes are immune-related and several are known to be important transcription factors, adhesion molecules, and cytokines, such as NF-kappa B p105 and p49/p100, C/EBP beta and delta, SOCS3, CD83, CD44, ICAM-1, TNF-alpha, IL-1 beta, Mip1-alpha, Mip1-beta, MCP-1, and RANTES. Additionally, we identified several apoptosis-associated genes that were significantly up-regulated by Act-treatment, which included GADD45, TDAG51, TRAF1, BIM, and JunB. While it is known that Act leads to cell death, the mechanism of cell death is unknown. The data presented here strongly suggests that Act induces macrophage apoptosis, which could contribute significantly to the disease process. **Principal component analysis** revealed two major trends in the data: a reproducible subset of genes that were up-regulated early and a second subset of genes that were up-regulated after 2 hr. In order to identify groups of genes with similar expression patterns, we performed hierarchical and K means clustering using five separate clustering algorithms, each of which produced a similar clustered set of immune response-related genes that were up-regulated by 2 hr. The array data generated by this study provides a global view of Act-mediated signal transduction and clearly demonstrates an inflammatory response to this toxin at the molecular level.

L3 ANSWER 7 OF 10 MEDLINE on STN DUPLICATE 2
AN 2002677880 MEDLINE
DN PubMed ID: 12437328
TI Analytical reproducibility in (1)H NMR-based metabonomic urinalysis.
AU Keun Hector C; Ebbels Timothy M D; Antti Henrik; Bollard Mary E; Beckonert Olaf; Schlotterbeck Gotz; Senn Hans; Niederhauser Urs; Holmes Elaine; Lindon John C; Nicholson Jeremy K
CS Biological Chemistry, Biomedical Sciences, Faculty of Medicine, Imperial College of Science, Technology and Medicine, London, SW7 2AZ, UK.. h.keun@ic.ac.uk
SO Chemical research in toxicology, (2002 Nov) 15 (11) 1380-6.
Journal code: 8807448. ISSN: 0893-228X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200306
ED Entered STN: 20021120
Last Updated on STN: 20030621
Entered Medline: 20030620
AB Metabonomic analysis of biofluids and tissues utilizing high-resolution NMR spectroscopy and chemometric techniques has proven valuable in characterizing the biochemical response to **toxicity** for many xenobiotics. To assess the analytical reproducibility of metabonomic protocols, sample preparation and NMR data acquisition were performed at two sites (one using a 500 MHz and the other using a 600 MHz system) using two identical (split) sets of urine samples from an 8-day acute study of hydrazine **toxicity** in the rat. Despite the difference in spectrometer operating frequency, both datasets were extremely similar when analyzed using **principal components analysis** (PCA) and gave near-identical descriptions of the metabolic responses to hydrazine treatment. The main consistent difference between the datasets was related to the efficiency of water resonance suppression in the spectra. In a 4-PC model of both datasets combined, describing all systematic dose- and time-related variation (88% of the total variation), differences between the two datasets accounted for only 3% of the total modeled variance compared to ca. 15% for normal physiological (pre-dose) variation. Furthermore, <3% of spectra displayed distinct inter-site differences, and these were clearly identified as

outliers in their respective dose-group PCA models. No samples produced clear outliers in both datasets, suggesting that the outliers observed did not reflect an unusual sample composition, but rather sporadic differences in sample preparation leading to, for example, very dilute samples. Estimations of the relative concentrations of citrate, hippurate, and taurine were in >95% correlation (r(2)) between sites, with an analytical error comparable to normal physiological variation in concentration (4-8%). The excellent analytical reproducibility and robustness of metabonomic techniques demonstrated here are highly competitive compared to the best proteomic analyses and are in significant contrast to genomic **microarray** platforms, both of which are complementary techniques for predictive and mechanistic **toxicology**. These results have implications for the quantitative interpretation of metabonomic data, and the establishment of quality control criteria for both regulatory agencies and for integrating data obtained at different sites.

L3 ANSWER 8 OF 10 MEDLINE on STN DUPLICATE 3
AN 2002431552 MEDLINE
DN PubMed ID: 12187938
TI Methapyrilene **toxicity**: anchorage of pathologic observations to gene expression alterations.
AU Hamadeh Hisham K; Knight Brian L; Haugen Astrid C; Sieber Stella; Amin Rupesh P; Bushel Pierre R; Stoll Raymond; Blanchard Kerry; Jayadev Supriya; Tennant Raymond W; Cunningham Michael L; Afshari Cynthia A; Paules Richard S
CS National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina 27709, USA.
SO Toxicologic pathology, (2002 Jul-Aug) 30 (4) 470-82.
Journal code: 7905907. ISSN: 0192-6233.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200303
ED Entered STN: 20020822
Last Updated on STN: 20030313
Entered Medline: 20030312
AB Methapyrilene (MP) exposure of animals can result in an array of adverse pathological responses including hepatotoxicity. This study investigates gene expression and histopathological alterations in response to MP treatment in order to 1) utilize computational approaches to classify samples derived from livers of MP treated rats based on severity of **toxicity** incurred in the corresponding tissue, 2) to phenotypically anchor gene expression pattems, and 3) to gain insight into mechanism(s) of methapyrilene hepatotoxicity. Large-scale differential gene expression levels associated with the exposure of male Sprague-Dawley rats to the rodent hepatic carcinogen MP for 1, 3, or 7 days after daily dosage with 10 or 100 mg/kg/day were monitored. Hierarchical clustering and **principal component analysis** were successful in classifying samples in agreement with microscopic observations and revealed low-dose effects that were not observed histopathologically. Data from cDNA **microarray** analysis corroborated observed histopathological alterations such as hepatocellular necrosis, bile duct hyperplasia, microvesicular vacuolization, and portal inflammation observed in the livers of MP exposed rats and provided insight into the role of specific genes in the studied **toxicological** processes.

L3 ANSWER 9 OF 10 MEDLINE on STN DUPLICATE 4
AN 2002272784 MEDLINE
DN PubMed ID: 12011482
TI Prediction of compound signature using high density gene expression

profiling.
CM Comment in: Toxicol Sci. 2002 Jun;67(2):155-6. PubMed ID: 12011473
AU Hamadeh Hisham K; Bushel Pierre R; Jayadev Supriya; DiSorbo Olimpia; Bennett Lee; Li Leping; Tennant Raymond; Stoll Raymond; Barrett J Carl; Paules Richard S; Blanchard Kerry; Afshari Cynthia A
CS National Institute of Environmental Health Sciences, P.O. Box 12233, MD2-04, Research Triangle Park, NC 27709, USA.
SO Toxicological sciences : an official journal of the Society of Toxicology, (2002 Jun) 67 (2) 232-40.
Journal code: 9805461. ISSN: 1096-6080.
CY United States
DT (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200210
ED Entered STN: 20020516
Last Updated on STN: 20021011
Entered Medline: 20021010
AB DNA **microarrays**, used to measure the gene expression of thousands of genes simultaneously, hold promise for future application in efficient screening of therapeutic drugs. This will be aided by the development and population of a database with gene expression profiles corresponding to biological responses to exposures to known compounds whose **toxicological** and pathological endpoints are well characterized. Such databases could then be interrogated, using profiles corresponding to biological responses to drugs after developmental or environmental exposures. A positive correlation with an archived profile could lead to some knowledge regarding the potential effects of the tested compound or exposure. We have previously shown that cDNA **microarrays** can be used to generate chemical-specific gene expression profiles that can be distinguished across and within compound classes, using clustering, simple correlation, or **principal component analyses**. In this report, we test the hypothesis that knowledge can be gained regarding the nature of blinded samples, using an initial training set comprised of gene expression profiles derived from rat liver exposed to clofibrate, Wyeth 14,643, gemfibrozil, or phenobarbital for 24 h or 2 weeks of exposure. Highly discriminant genes were derived from our database training set using approaches including linear discriminant analysis (LDA) and genetic algorithm/K-nearest neighbors (GA/KNN). Using these genes in the analysis of coded liver RNA samples derived from 24-h, 3-day, or 2-week exposures to phenytoin, diethylhexylpthalate, or hexobarbital led to successful prediction of whether these samples were derived from livers of rats exposed to enzyme inducers or to peroxisome proliferators. This validates our initial hypothesis and lends credibility to the concept that the further development of a gene expression database for chemical effects will greatly enhance the hazard identification processes.

L3 ANSWER 10 OF 10 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2001:240653 BIOSIS
DN PREV200100240653
TI Genomics and proteomics: The new millennium of drug discovery and development.
AU Cunningham, Mary Jane [Reprint author]
CS Genometrix, Inc., 2700 Research Forest Drive, The Woodlands, TX, 77381, USA
mcunningham@genometrix.com
SO Journal of Pharmacological and Toxicological Methods, (July-August, 2000) Vol. 44, No. 1, pp. 291-300. print.
CODEN: JPTMEZ. ISSN: 1056-8719.
DT Article

LA English
ED Entered STN: 16 May 2001
Last Updated on STN: 18 Feb 2002
AB One of the most pressing issues facing the pharmaceutical and biotechnology industry is the tremendous dropout rate of lead drug candidates. Over the last two decades, several new genomic technologies have been developed in hopes of addressing the issues of target identification and lead candidate optimization. Gene expression **microarray** is one of these technologies and this review describes the four main formats, which are currently available: (a) cDNA; (b) oligonucleotide; (c) electrokinetic; and (d) fiberoptic. Many of these formats have been developed with the goal of screening large numbers of genes. Recently, a high-throughput array format has been developed where a large number of samples can be assayed using arrays in parallel. In addition, focusing on gene expression may be only one avenue in preventing lead candidate failure. Proteomics or the study of protein expression may also play a role. Two-dimensional polyacrylamide gel electrophoresis (2-DE) coupled with mass spectroscopy has been the most widely accepted format to study protein expression. However, protein **microarrays** are now being developed and modified to a high-throughput screening format. Examples of several gene and protein expression studies as they apply to drug discovery and development are reviewed. These studies often result in large data sets. Examples of how several statistical methods (**principal components analysis** (PCA), clustering methods, Shannon entropy, etc.) have been applied to these data sets are also described. These newer genomic and proteomic technologies and their analysis and visualization methods have the potential to make the drug discovery and development process less costly and more efficient by aiding to select better target and lead candidates.

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(FILE 'HOME' ENTERED AT 14:59:29 ON 18 MAR 2004)

FILE 'MEDLINE, BIOSIS' ENTERED AT 15:12:54 ON 18 MAR 2004
L1 133 S PRINCIPAL COMPONENT ANALYSIS AND MICROARRAY
L2 14 S L1 AND TOXIC?
L3 10 DUPLICATE REMOVE L2 (4 DUPLICATES REMOVED)

=> s l1 and review/dt
L4 2 L1 AND REVIEW/DT

=> d 1-2 bib ab

L4 ANSWER 1 OF 2 MEDLINE on STN
AN 2002316752 MEDLINE
DN PubMed ID: 12058619
TI Multiscale and Bayesian approaches to data analysis in genomics high-throughput screening.
AU Yang Chihae; Bakshi Bhavik R; Rathman James F; Blower Paul E Jr
CS LeadScope Inc, 1245 Kinnear Road, Columbus, OH 43212, USA.. cyang@leadscope.com
SO Current opinion in drug discovery & development, (2002 May) 5 (3) 428-38. Ref: 37
Journal code: 100887519. ISSN: 1367-6733.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals

EM 200211
ED Entered STN: 20020613
Last Updated on STN: 20021214
Entered Medline: 20021126
AB Tremendous amounts of data are produced by high-throughput screening methods currently employed in drug discovery and product development. A typical cDNA **microarray** or oligonucleotide-based gene chip experiment easily generates over 10,000 data points for each array or chip. The challenge of inferring meaningful information is formidable given the size and number of these datasets. This paper reviews the current status of statistical tools available for gene expression analysis, with emphasis on Bayesian approaches and multiscale wavelet filtering. Fundamental concepts of Bayesian and multiscale modeling are discussed from the perspective of their potential to address important issues related to the analysis of gene expression data, such as the fact that genomic data often have non-Gaussian distributions and feature localization and multiple scales in both frequency and measurement dimension. Recent publications in these areas are reviewed. Wavelet filtering and the advantages of multiscale methods are demonstrated by application to publicly available gene expression data from the National Cancer Institute (NCI). Multiscale methods, including multiscale **principal component analysis** (MSPCA), are applied to extract gene subsets and to visualize data in multidimensions for comparisons. Similarity in cell lines and gene selection are effectively visualized and quantitatively compared.

L4 ANSWER 2 OF 2 MEDLINE on STN
AN 2001186706 MEDLINE
DN PubMed ID: 11274896
TI Genomics and proteomics: the new millennium of drug discovery and development.
CM Erratum in: J Pharmacol Toxicol Methods 2001 Jan-Feb;45(1):85
AU Cunningham M J
CS Genometrix, Inc., 2700 Research Forest Drive, The Woodlands, TX 77381, USA.. mcunningham@genometrix.com
SO Journal of pharmacological and toxicological methods, (2000 Jul-Aug) 44 (1) 291-300. Ref: 120
Journal code: 9206091. ISSN: 1056-8719.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200105
ED Entered STN: 20010521
Last Updated on STN: 20011105
Entered Medline: 20010517
AB One of the most pressing issues facing the pharmaceutical and biotechnology industry is the tremendous dropout rate of lead drug candidates. Over the last two decades, several new genomic technologies have been developed in hopes of addressing the issues of target identification and lead candidate optimization. Gene expression **microarray** is one of these technologies and this review describes the four main formats, which are currently available: (a) cDNA; (b) oligonucleotide; (c) electrokinetic; and (d) fiberoptic. Many of these formats have been developed with the goal of screening large numbers of genes. Recently, a high-throughput array format has been developed where a large number of samples can be assayed using arrays in parallel. In addition, focusing on gene expression may be only one avenue in preventing lead candidate failure. Proteomics or the study of protein expression may also play a role. Two-dimensional polyacrylamide gel electrophoresis

(2-DE) coupled with mass spectroscopy has been the most widely accepted format to study protein expression. However, protein **microarrays** are now being developed and modified to a high-throughput screening format. Examples of several gene and protein expression studies as they apply to drug discovery and development are reviewed. These studies often result in large data sets. Examples of how several statistical methods (**principal components analysis** [PCA], clustering methods, Shannon entropy, etc.) have been applied to these data sets are also described. These newer genomic and proteomic technologies and their analysis and visualization methods have the potential to make the drug discovery and development process less costly and more efficient by aiding to select better target and lead candidates.

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     (FILE 'HOME' ENTERED AT 14:59:29 ON 18 MAR 2004)

     FILE 'MEDLINE, BIOSIS' ENTERED AT 15:12:54 ON 18 MAR 2004
L1          133 S PRINCIPAL COMPONENT ANALYSIS AND MICROARRAY
L2           14 S L1 AND TOXIC?
L3           10 DUPLICATE REMOVE L2 (4 DUPLICATES REMOVED)
L4            2 S L1 AND REVIEW/DT

=> s l1 and py<2001
L5           10 L1 AND PY<2001

=> duplicate remove l5
DUPLICATE PREFERENCE IS 'MEDLINE, BIOSIS'
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L6            8 DUPLICATE REMOVE L5 (2 DUPLICATES REMOVED)

=> d 1-8 bib ab

L6   ANSWER 1 OF 8  BIOSIS  COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN   2001:355525  BIOSIS
DN   PREV200100355525
TI   Information processing issues and solutions associated with
     microarray technology.
AU   Zhou, Yi-Xiong [Reprint author]; Kalocsai, Peter [Reprint author]; Chen,
     Jing-Ying [Reprint author]; Shams, Soheil [Reprint author]
CS   BioDiscovery, Inc., Los Angeles, CA, USA
SO   Schena, Mark. (2000) pp. 167-200. Microarray biochip technology. print.
     Publisher: Eaton Publishing, 154 E. Central Street, Natick, MA, 01760,
     USA.
     ISBN: 1-881299-37-6 (cloth).
DT   Book
     Book; (Book Chapter)
LA   English
ED   Entered STN: 2 Aug 2001
     Last Updated on STN: 19 Feb 2002

L6   ANSWER 2 OF 8     MEDLINE on STN                    DUPLICATE 1
AN   2000259437     MEDLINE
DN   PubMed ID: 10797298
TI   Classification of human ovarian tumors using multivariate data analysis of
     polypeptide expression patterns.
AU   Alaiya A A; Franzen B; Hagman A; Silfversward C; Moberger B; Linder S;
     Auer G
CS   Unit of Cell and Molecular Analysis, Department of Oncology and Pathology,
     Karolinska Institute and Hospital, Stockholm, Sweden..
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Alaiya.Ayodele@cck.ki.se
SO International journal of cancer. Journal international du cancer, **(2000 Jun 1)** 86 (5) 731-6.
Journal code: 0042124. ISSN: 0020-7136.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200006
ED Entered STN: 20000616
Last Updated on STN: 20000616
Entered Medline: 20000608
AB Large amounts of data on quantitative gene expression are generated by procedures such as 2-DE analysis of proteins or cDNA **microarrays** . Quantitative molecular variation may potentially be used for the development of methods for the classification of tumors. We used here the statistical concepts of **principal components analysis** (PCA) and partial least square analysis (PLS) in an attempt to type ovarian tumors. Using a set of 170 polypeptides, 22 tumors were used to establish a model ("learning set") for classification into 3 groups (benign/borderline/malignant). Eighteen tumors were then used to test the model. Six of 8 carcinomas and 3 of 4 borderline tumors were correctly classified. Two of 6 benign lesions were correctly classified, 3 were classified as borderline and 1 as carcinoma. We conclude that it may be possible to classify tumors according to their constitutive protein expression profile using multivariate analysis, thus making classification by artificial intelligence a future possibility. Copyright 2000 Wiley-Liss, Inc.

L6 ANSWER 3 OF 8 MEDLINE on STN
AN 2000410548 MEDLINE
DN PubMed ID: 10902193
TI **Principal components analysis** to summarize **microarray** experiments: application to sporulation time series.
AU Raychaudhuri S; Stuart J M; Altman R B
CS Stanford Medical Informatics, Stanford University, CA 94305-5479, USA.. sxr@smi.stanford.edu
NC GM-07365 (NIGMS)
LM-07033 (NLM)
LM06244 (NLM)
SO Pacific Symposium on Biocomputing. Pacific Symposium on Biocomputing, **(2000)** 455-66.
Journal code: 9711271.
CY Singapore
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200008
ED Entered STN: 20000907
Last Updated on STN: 20000907
Entered Medline: 20000829
AB A series of **microarray** experiments produces observations of differential expression for thousands of genes across multiple conditions. It is often not clear whether a set of experiments are measuring fundamentally different gene expression states or are measuring similar states created through different mechanisms. It is useful, therefore, to define a core set of independent features for the expression states that allow them to be compared directly. **Principal components analysis** (PCA) is a statistical technique for determining the key variables in a multidimensional data set that explain the differences in the observations, and can be used to simplify the analysis and visualization of multidimensional data sets. We show that

application of PCA to expression data (where the experimental conditions are the variables, and the gene expression measurements are the observations) allows us to summarize the ways in which gene responses vary under different conditions. Examination of the components also provides insight into the underlying factors that are measured in the experiments. We applied PCA to the publicly released yeast sporulation data set (Chu et al. 1998). In that work, 7 different measurements of gene expression were made over time. PCA on the time-points suggests that much of the observed variability in the experiment can be summarized in just 2 components--i.e. 2 variables capture most of the information. These components appear to represent (1) overall induction level and (2) change in induction level over time. We also examined the clusters proposed in the original paper, and show how they are manifested in principal component space. Our results are available on the internet at http: www.smi.stanford.edu/project/helix/PCArray .

L6 ANSWER 4 OF 8 MEDLINE on STN DUPLICATE 2
AN 2001186706 MEDLINE
DN PubMed ID: 11274896
TI Genomics and proteomics: the new millennium of drug discovery and development.
CM Erratum in: J Pharmacol Toxicol Methods 2001 Jan-Feb;45(1):85
AU Cunningham M J
CS Genometrix, Inc., 2700 Research Forest Drive, The Woodlands, TX 77381, USA.. mcunningham@genometrix.com
SO Journal of pharmacological and toxicological methods, **(2000 Jul-Aug)** 44 (1) 291-300. Ref: 120
Journal code: 9206091. ISSN: 1056-8719.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200105
ED Entered STN: 20010521
Last Updated on STN: 20011105
Entered Medline: 20010517
AB One of the most pressing issues facing the pharmaceutical and biotechnology industry is the tremendous dropout rate of lead drug candidates. Over the last two decades, several new genomic technologies have been developed in hopes of addressing the issues of target identification and lead candidate optimization. Gene expression **microarray** is one of these technologies and this review describes the four main formats, which are currently available: (a) cDNA; (b) oligonucleotide; (c) electrokinetic; and (d) fiberoptic. Many of these formats have been developed with the goal of screening large numbers of genes. Recently, a high-throughput array format has been developed where a large number of samples can be assayed using arrays in parallel. In addition, focusing on gene expression may be only one avenue in preventing lead candidate failure. Proteomics or the study of protein expression may also play a role. Two-dimensional polyacrylamide gel electrophoresis (2-DE) coupled with mass spectroscopy has been the most widely accepted format to study protein expression. However, protein **microarrays** are now being developed and modified to a high-throughput screening format. Examples of several gene and protein expression studies as they apply to drug discovery and development are reviewed. These studies often result in large data sets. Examples of how several statistical methods (**principal components analysis** [PCA], clustering methods, Shannon entropy, etc.) have been applied to these data sets are also described. These newer genomic and proteomic technologies and their analysis and visualization methods have the potential to make

the drug discovery and development process less costly and more efficient by aiding to select better target and lead candidates.

L6 ANSWER 5 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2000:478916 BIOSIS
DN PREV200000478916
TI Hierarchical agglomerative nesting of gene expression levels from cDNA **microarrays**.
AU Peterson, Leif E. [Reprint author]
CS Department of Medicine, Baylor College of Medicine, Houston, TX, USA
SO Genetic Epidemiology, (October, 2000) Vol. 19, No. 3, pp. 269. print.
Meeting Info.: Ninth Annual Meeting of the International Genetic Epidemiology Society. San Antonio, Texas, USA. October 27-28, 2000.
ISSN: 0741-0395.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 8 Nov 2000
Last Updated on STN: 10 Jan 2002

L6 ANSWER 6 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2001:516870 BIOSIS
DN PREV200100516870
TI Data visualization and analysis tools for high density **microarrays**.
AU Saeed, Alexander I. [Reprint author]; Sturn, Alexander [Reprint author]; Quackenbush, John [Reprint author]
CS Institute for Genomic Research, Rockville, MD, USA
SO International Genome Sequencing and Analysis Conference, (2000) Vol. 12, pp. 105. print.
Meeting Info.: 12th International Genome Sequencing and Analysis Conference. Miami Beach, Florida, USA. September 12-15, 2000.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 7 Nov 2001
Last Updated on STN: 23 Feb 2002
AB **Microarrays** provide the opportunity to study gene expression patterns on a genomic scale. Thousands of genes are arrayed on a microscope slide and relative expression levels are determined by measuring fluorescence intensity of labeled mRNA hybridized to the arrays. We have developed a package of Java based tools to facilitate the analysis of this data, allowing the user to display graphical representations of hybridized slides, perform statistical tests to identify differentially expressed or similar genes, and view and export the results. Expression data is read from flat files or a relational database, via JDBC, as single slides or a series of experiments. A representation of the hybridizations is generated, showing a grid of experiments and genes, where multiple experiments can easily be compared with each other. A detail view focusing on a single slide is available, showing each spot as a rectangle in its appropriate location on the slide. In both displays, elements are colored to represent relative expression, based on several options including two split-ratio displays, green/red overlay and false color. Clicking on an element will allow the user to access information about the underlying gene. Fluorescence intensities can be normalized using a number of strategies. Differentially expressed genes can be identified using a variety of statistical tests. Several types of gene and experiment analyses have been facilitated, including hierarchical and K-means clustering, self-organizing maps, **principal component analysis** and support vector machines. All results are shown in various graphical representations to provide better

visibility of the underlying patterns. Other display tools include scatterplot displays of expression measurements and histograms of various expression ratio frequencies.

L6 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2001:75809 BIOSIS
DN PREV200100075809
TI Massive gene expression profiling in an in vivo model of ischemic preconditioning.
AU Melcher, T. [Reprint author]; Mueller, S.; McFarland, K. C.; Chin, D.; Hendrix, D.; Zhao, O.; Melero, C.; Steger, C.; Gido, G.; Wieloch, T.
CS Agy Therapeutics, South San Francisco, CA, USA
SO Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-12.1. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 04-09, 2000. Society for Neuroscience.
ISSN: 0190-5295.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 7 Feb 2001
Last Updated on STN: 12 Feb 2002
AB In the CA1 field of the hippocampus, a brief episode of ischemia induces mechanisms that protect neurons from the lethal effects of prolonged ischemia. The molecular mechanisms underlying this phenomenon are poorly understood. We have analyzed changes in gene expression in CA1 fields at various timepoints following the induction of ischemic preconditioning by combining de novo differential cloning with cDNA **microarray** techniques. Over 2,000 genes, many without recognized function, were identified as induced at different timepoints. **Principal component analysis** of **microarray** data was used to derive both spatial and temporal gene expression patterns in various ischemia models, brain regions and peripheral tissues. The results suggest the involvement of many different signaling pathways in the establishment of ischemic preconditioning and point to a small number of genes as key players in the neuroprotective process.

L6 ANSWER 8 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1999:161251 BIOSIS
DN PREV199900161251
TI Protein detection using conducting polymer **microarrays**.
AU Lu, W.; Nguyen, T. A.; Wallace, Gordon G. [Reprint author]
CS Intelligent Polymer Res. Inst., Univ. Wollongong, Northfields Avenue, Wollongong, NSW 2522, Australia
SO Electroanalysis, (Nov., 1998) Vol. 10, No. 16, pp. 1101-1107. print.
CODEN: ELANEU. ISSN: 1040-0397.
DT Article
LA English
ED Entered STN: 16 Apr 1999
Last Updated on STN: 16 Apr 1999
AB An array of conducting polymer coated microelectrodes was employed as an amperometric detector to analyze a range of proteins. Using conducting polymer coatings with different counterions incorporated, varying selectivity series have been obtained. Protein identification and quantification were performed using chemometric techniques such as **principal component analysis** (PCA), soft independent modelling of class analogy (SIMCA), ordinary least square (OLS) and partial least square (PLS). Using four different polymers, response patterns were obtained and classification of six proteins was achieved. Individual proteins in a two-component mixture were quantitatively analyzed with acceptable accuracy.

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NEWS 4	DEC 08	INPADOC: Legal Status data reloaded
NEWS 5	SEP 29	DISSABS now available on STN
NEWS 6	OCT 10	PCTFULL: Two new display fields added
NEWS 7	OCT 21	BIOSIS file reloaded and enhanced
NEWS 8	OCT 28	BIOSIS file segment of TOXCENTER reloaded and enhanced
NEWS 9	NOV 24	MSDS-CCOHS file reloaded
NEWS 10	DEC 08	CABA reloaded with left truncation
NEWS 11	DEC 08	IMS file names changed
NEWS 12	DEC 09	Experimental property data collected by CAS now available in REGISTRY
NEWS 13	DEC 09	STN Entry Date available for display in REGISTRY and CA/CAplus
NEWS 14	DEC 17	DGENE: Two new display fields added
NEWS 15	DEC 18	BIOTECHNO no longer updated
NEWS 16	DEC 19	CROPU no longer updated; subscriber discount no longer available
NEWS 17	DEC 22	Additional INPI reactions and pre-1907 documents added to CAS databases
NEWS 18	DEC 22	IFIPAT/IFIUDB/IFICDB reloaded with new data and search fields
NEWS 19	DEC 22	ABI-INFORM now available on STN
NEWS 20	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS 21	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS 22	FEB 05	German (DE) application and patent publication number format changes
NEWS 23	MAR 03	MEDLINE and LMEDLINE reloaded
NEWS 24	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS 25	MAR 03	FRANCEPAT now available on STN

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NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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